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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	SINGH *et al.*	Atty. Dkt. No.:	RLL-475US
Serial No.:	10/596,013	Group Art Unit:	Unknown
Filing Date:	May 25, 2006	Examiner:	Unknown

Title: PHARMACEUTICAL COMPOSITIONS COMPRISING NATEGLINIDE AND A SURFACTANT

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Kim Campbell

Kim Campbell

Commissioner of Patents
P.O. Box 1450
Alexandria, VA 22313-1450

TRANSMISSION OF PRIORITY DOCUMENT

Applicants transmit herewith a certified copy of Indian Patent Application No. 1497/Del/2003 filed 28 November 2003 (28.November.2003) to which priority is claimed herein.

Respectfully submitted,

RANBAXY LABORATORIES LIMITED

By: _____

Jayadeep R. Deshmukh
Vice President - Intellectual Property

Dated: May 30, 2007

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I, the undersigned being an officer duly authorized in accordance with the provision of the Patent Act, 1970 hereby certify that annexed hereto is the true copy of the ***Application, and Complete Specification*** *filed in connection with* ***Patent Application No. 1497/Del/2003 Dated 28th November, 2003.***

Witness my hand this 3rd day of April ,2007

(N.R.Meena)
Assistant Controller Of Patents & Designs

1497 DEL 03

FORM 1

THE PATENTS ACT, 1970

(39 of 1970)

28 NOV 2003

Received 3000/-
5993

APPLICATION FOR GRANT OF A PATENT

(See Sections 5(2), 7, 54 and 135; and rule 39)

1 We, **RANBAXY LABORATORIES LIMITED**, a Company incorporated under the Companies Act, 1956, Corporate Office at 19, Nehru Place, New Delhi - 110 019, India

2. hereby declare –

(a) that we are in possession of an invention titled **"PHARMACEUTICAL COMPOSITIONS COMPRISING NATEGLINIDE IN COMBINATION WITH A SURFACTANT"**

(b) that the Complete Specification relating to this invention is filed with this application.

(c) that there is no lawful ground of objection to the grant of a patent to us.

3. Further declare that the inventors for the said invention are

a. ROMI BARAT SINGH
b. ANU SHILPA
c. VISHNUBHOTLA NAGA PRASAD
d. SANJEEV KUMAR SETHI

of Ranbaxy Laboratories Limited, Plot No. 20, Sector-18, Udyog Vihar Industrial Area, Gurgaon – 122001 (Haryana), India, all Indian Nationals.

4. We claim the priority from the application(s) filed in convention countries, particulars of which are as follows: **NOT APPLICABLE**

5. We state that the said invention is an improvement in or modification of the invention, the particulars of which are as follows and of which we are the applicant: : **NOT APPLICABLE**

6. We state that the application is divided out of our application, the particulars of which are given below and pray that this application deemed to have been filed on ..... Under section 16 of the Act. **NOT APPLICABLE**

7. That we are the assignee or legal representatives of the true and first inventors.

8. That our address for service in India is as follows:

DR. B. VIJAYARAGHAVAN
Associate Director – Intellectual Property
Ranbaxy Laboratories Limited
Plot No.20, Sector – 18, Udyog Vihar Industrial Area,
Gurgaon – 122001 (Haryana). INDIA.
Tel. No. (91-124) 2343126, 2342001–10; 5012501-10

9. Following declaration was given by the inventors or applicants in the convention country:

We, ROMI BARAT SINGH, ANU SHILPA, VISHNUBHOTLA NAGA PRASAD, SANJEEV KUMAR SETHI of Ranbaxy Laboratories Limited, Plot No. 20, Sector – 18, Udyog Vihar Industrial Area, Gurgaon–122001 (Haryana), India, all Indian Nationals, the true and first inventors for this invention or applicant in the convention country declare that the applicant herein, **Ranbaxy Laboratories Limited**, Corporate Office at 19, Nehru Place, New Delhi - 110 019, India, is our assignee or legal representatives.

a. Romi Singh
(ROMI BARAT SINGH)

b. Shilpa.
(ANU SHILPA)

c.
(VISHNUBHOTLA NAGA PRASAD)

d.
(SANJEEV KUMAR SETHI)

10. That to the best of our knowledge, information and belief the fact and matters stated herein are correct and that there is no lawful ground of objection to the grant of patent to us on this application.

11. Followings are the attachment with the application:
   a. Provisional Specification (3 copies)
   b. Drawings (3 copies)
   c. Priority document(s)
   d. Statement and Undertaking on FORM – 3
   e. Power of Authority (Not required)
   f. Fee Rs.**3,000**/- (Rupees Three Thousand only..) in cheque bearing No. dated : drawn on **HDFC Bank Limited, New Delhi.**

We request that a patent may be granted to us for the said invention.

Dated this **28TH** day of **November, 2003.**

For Ranbaxy Laboratories Limited

(SUSHIL KUMAR PATAWARI)
Company Secretary

FORM 2

The Patents Act, 1970

(39 of 1970)

COMPLETE SPECIFICATION

(See Section 10)

PHARMACEUTICAL COMPOSITIONS COMPRISING NATEGLINIDE IN COMBINATION WITH A SURFACTANT

RANBAXY LABORATORIES LIMITED

19, NEHRU PLACE, NEW DELHI - 110019

A Company incorporated under the Companies Act, 1956.

The following specification particularly describes and ascertains the nature of this invention and the manner in which it is to be performed:

The present invention relates to pharmaceutical compositions comprising Nateglinide in combination with a surfactant.

Nateglinide is an amino acid derivative that lowers blood glucose levels by stimulating insulin secretion from the pancreas. It is widely indicated as monotherapy to lower blood glucose in patients with Type 2 diabetes. It is also indicated for use in combination with Metformin.

Presently Nateglinide oral tablets are available in 60mg or 120mg strengths and are marketed by Novartis under the trade name STARLIX.

As the active agent, Nateglinide is described in EP 196222 and EP 526171. The active agent can be present as its pharmaceutically acceptable salts selected from acid addition salts, for example, as a sodium salt or as a maleate or hydrochloride.

Nateglinide has a poor solubility, hence the desired dissolution is difficult to achieve.

Prior art patent US 6,559,188 describe compositions of Nateglinide or a pharmaceutically acceptable salt thereof. All the examples given in US 6559188 make use of combination of water-soluble and water insoluble filler.

US 2003/0021843 discloses an antidiabetic preparation for oral administration containing nateglinide and at least one material selected from the group consisting of polysaccharides, polyacrylic acids, polylactic acids, polyoxyethylene, polyvinyl pyrrolidone, polyvinyl alcohol, oils and surfactants. Nateglinide being dispersed in the material or being emulsified or microencapsulated or coated with the material prepares the compositions. In this application the combination of oil and surfactant is used for the preparation of emulsions.

The use of surfactants in pharmaceutical formulations to assist in disintegration and dissolution of drug material is well known. Lachman et al., Theory and Practice of Industrial Pharmacy, Second Edition, pp. 108-9, disclose the use of surface active agents or "surfactants" in almost every dosage form including liquids, semi-solids and solids. The surfactants play an important role in the absorption and efficacy of certain drugs.

The invention is directed to a surprising and unexpected discovery of use of surfactants to enhance the solubility and dissolution of solid dose oral formulations of poorly soluble drugs like Nateglinide.

Present invention provides more flexibility and choice of pharmaceutical excipients like binders and fillers.

Surfactants usable in the present invention can be anionic, nonionic, or cationic in nature as well as mixtures of these.

Hence in one aspect it provides an oral solid composition comprising Nateglinide in a free or pharmaceutically acceptable salt form and a surfactant, which reduces surface tension of the medium in which it is dissolved and/or interfacial tension with other phases.

In another aspect it provides an oral solid composition comprising Nateglinide in a free or pharmaceutically acceptable salt form and a surfactant wherein the surfactant is selected from a group of anionic, nonionic, or cationic or a combination thereof.

In another aspect it provides an oral solid composition comprising Nateglinide in a free or pharmaceutically acceptable salt form and a surfactant wherein the surfactant is selected from anionic surfactants such as sodium lauryl sulphate, potassium dodecyl sulphonate, sodium dodecyl benzene sulphonate, sodium salt of lauryl polyoxyethylene sulphate, lauryl polyethylene oxide sulfonate, dioctyl ester of sodium sulphosuccinic acid or sodium lauryl sulphonate and the like.

In another aspect it provides an oral solid composition comprising Nateglinide in a free or pharmaceutically acceptable salt form and a surfactant wherein the surfactant is selected from nonionic surfactants such as polysorbate 80, nonyl phenol polyoxyethylene ether, tridecyl alcohol polyoxyethylene ether, dodecyl mercaptan polyoxyethylene thioether, the lauric ester of polyethylene glycol, the lauric ester of sorbitan polyoxyethylene ether or tertiary alkyl amine oxide and the like.

In another aspect it provides an oral solid composition comprising Nateglinide in a free or pharmaceutically acceptable salt form and a surfactant wherein the surfactant is selected from cationic surfactants such as distearyl dimethyl ammonium chloride, stearyl dimethyl benzyl ammonium chloride, stearyl trimethyl ammonium chloride, coco dimethyl benzyl ammonium chloride, dicoco dimethyl ammonium chloride, cetyl pyridinium chloride, cetyl trimethyl ammonium bromide, stearyl amine salts that are soluble in water such as stearyl amine acetate and stearyl amine hydrochloride, stearyl dimethyl amine hydrochloride, distearyl amine hydrochloride, alklyl phenoxyethoxyethyl dimethyl ammonium chloride, decyl pyridinium bromide, pyridinium chloride derivative of the acetyl amino ethyl esters of lauric acid, lauryl trimethyl ammonium chloride, decyl amine acetate, lauryl dimethyl ethyl ammonium chloride, the lactic acid and citric acid and other acid salts of stearyl-1-amidoimidazoline with methyl chloride, benzyl chloride, chloroacetic acid and similar compounds, mixtures of the foregoing and the like.

In another aspect it provides an oral solid composition comprising Nateglinide in a free or pharmaceutically acceptable salt form; a surfactant and at least one other antidiabetic compound.

In another aspect it provides an oral solid composition comprising Nateglinide in a free or pharmaceutically acceptable salt form; a surfactant and at least one other antidiabetic compound selected from the group consisting of glitazones, sulfonyl urea derivatives and metformin in each case in free form or in form of a pharmaceutically acceptable salt thereof.

In another aspect it provides a method of preparing an oral solid composition comprising Nateglinide in a free or pharmaceutically acceptable salt form and a surfactant.

In another aspect it provides an oral solid composition comprising Nateglinide in a free or pharmaceutically acceptable salt form and a surfactant for the preparation of a medicament for the prevention, delay of progression or treatment of metabolic disorders, in particular of type 2 diabetes mellitus or a disease or condition associated with diabetes mellitus.

The oral solid composition as described herein may include other pharmaceutically acceptable excipients in addition to Nateglinide and surfactant.

The term 'Nateglinide' as used herein includes Nateglinide in a free or pharmaceutically acceptable salt form such as an acid addition salt, for example as a sodium salt or as a maleate. In particular, the composition comprises the B- or H-type crystal modification of Nateglinide, more preferably the H-type. The active ingredient or a pharmaceutically acceptable salt thereof may also be used in form of a hydrate or include other solvents used for crystallization.

The dosage range of the nateglinide depends upon factors known to the person skilled in the art including species of the warm-blooded animal, body weight and age, the nature and severity of the condition to be treated, and the mode of administration to be employed. Unless stated otherwise herein, Nateglinide is preferably divided and administered from one to four times per day.

Nateglinide is preferably administered to the warm-blooded animal in a dosage in the range of about 5 to 1200, more preferably 10 to 1000 and most preferably 25 to 800 mg/day, especially when the warm-blooded animal is a human of about 70 kg body weight.

'Surfactants' as used herein includes a substance that lowers the surface tension of the medium in which it is dissolved, and/or the interfacial tension with other phases, and, accordingly, is positively adsorbed at the liquid/vapor and/or at other interfaces. Surfactants are classified into three groups: the anionics, nonionics and cationics; or a mixture of any of these compounds.

An anionic surfactant is the reaction product of an organic compound such as a high molecular weight acid or alcohol with an inorganic compound such as sodium hydroxide or sulfuric acid, yielding a product wherein the organic part of the molecule, or the water-insoluble part of the molecule, has a negative charge and the water-soluble part of the molecule wherein the sodium ion has a positive charge.

Nonionic surfactants have a hydrophobic/hydrophilic balance wherein there is neither a negative nor a positive charge in either part of the molecule, thus giving it the nonionic terminology.

Cationics surfactants are formed in reactions where alkyl halides react with primary, secondary, or tertiary fatty amines. Here the water-insoluble part of the molecule has a positive charge and the water-soluble part of the molecule is negatively charged, thus giving it the name of a cationic surface-active agent. Cationic surface-active agents reduce surface tension and are used as wetting agents in acid media.

The term 'other pharmaceutically acceptable excipient' refers to ingredients of the composition, excluding the active drug substance.

Examples of other pharmaceutically acceptable excipients as used herein include fillers, binders, disintegrants, lubricants, glidants, colors and the like.

The fillers can be selected from the group comprising of corn starch, lactose, white sugar, sucrose, sugar compressible, sugar confectioners, glucose, sorbitol, calcium carbonate, calcium phosphate-dibasic, calcium phosphate-tribasic, calcium sulfate, microcrystalline

cellulose, silicified microcrystalline cellulose, cellulose powdered, dextrates, dextrins, dextrose, fructose, kaolin, lactitol, mannitol, sorbitol, starch, starch pregelatinized and the like.

Examples of binders include methyl cellulose, hydroxypropyl cellulose, polyvinylpyrrolidone, gelatin, gum Arabic, ethyl cellulose, polyvinyl alcohol, pullulan, pregelatinized starch, agar, tragacanth, sodium alginate, propylene glycol, and the like.

Examples of disintegrants include starch, croscarmellose sodium, crospovidone, sodium starch glycolate and the like.

Examples of lubricants and glidants include colloidal anhydrous silica, stearic acid, magnesium stearate, calcium stearate, talc, hydrogenated castor oil, sucrose esters of fatty acids, microcrystalline wax, yellow beeswax, white beeswax and the like.

The coloring agents of the present invention may be selected from any FDA approved colors for oral use.

Nateglinide or pharmaceutically acceptable salt thereof may be present in any amount which is sufficient to elicit a therapeutic effect and, where applicable, may be present either substantially in the form of one optically pure enantiomer or as a mixture, racemic or otherwise, of enantiomers.

Nateglinide can be present in an amount of about 5% to about 70% (w/w), and most preferably about 15% to about 40% (w/w), based on the total weight of the dry composition.

The surfactants can be present in an amount of about 0.5% to about 10% (w/w), and most preferably about 1% to about 5% (w/w), by weight based on the total weight of the dry composition.

The oral solid composition can be prepared by processes known in the prior art such as wet granulation, dry granulation or direct compression and may be in the form of tablets or capsules.

In one of the embodiments nateglinide tablet may be prepared by blending nateglinide, surfactant, filler and disintegrant; granulating the blend with a binder solution; drying the granules; sizing; lubricating and compressing the lubricated granules.

In another embodiment nateglinide tablet may be prepared by blending nateglinide, surfactant, filler, disintegrant and binder; granulating the blend with a solvent; drying the granules; sizing; lubricating and compressing the lubricated granules.

Granulation may be carried out in fluidized bed dryer and sizing can be done by milling or pulverization.

In another embodiment nateglinide tablet may be prepared by blending nateglinide, surfactant, filler, disintegrant and binder; compacting or slugging the blend; breaking the slugs to make granules; lubricating and compressing the lubricated granules.

In another embodiment nateglinide tablet may be prepared by blending nateglinide, surfactant, filler, disintegrant, binder and lubricant; and compressing.

The tablets prepared by the present invention may be coated with one or more additional layers comprising film forming agents and/or pharmaceutically acceptable excipients.

The coating layers over the tablet may be applied as solution/ dispersion of coating ingredients using any conventional technique known in the prior art such as spray coating in a conventional coating pan or fluidized bed processor; dip coating and the like.

Example of solvents used for preparing a solution/dispersion of the coating ingredients include methylene chloride, isopropyl alcohol, acetone, methanol, ethanol, water and the like and mixtures thereof.

Example of film forming agents include ethyl cellulose, Hydroxypropyl methylcellulose, Hydroxypropyl cellulose, methyl cellulose, carboxymethylcellulose, hydroxymethylcellulose, hydroxyethylcellulose, hydroxypropyl methyl phthalate, cellulose acetate, cellulose acetate trimelliatate, cellulose acetate phthalate; Waxes such as polyethylene glycol; methacrylic acid polymers such as Eudragit ® RL and RS; and the like and mixture thereof. Alternatively, commercially available coating compositions comprising film-forming polymers marketed under various trade names, such as Opadry® may also be used for coating.

The following examples are illustrative of the invention, and are not to be construed as limiting the invention.

Example 1

Ingredient	**Quantity (wt/tablet) mg**
Nateglinide	121.21*
Lactose	424.16
Povidone	12
Croscarmellose sodium	20
Colloidal silicon dioxide	16
Purified water	q.s
Croscarmellose Sodium	12.8
Colloidal silicon dioxide	12.8
Magnesium stearate	11.4

** Equivalent to Nateglinide 120mg after potency and moisture adjustment*

PROCEDURE:

1. Nateglinide along with lactose, povidone, colloidal silicon dioxide and a part of croscarmellose sodium are mixed in a high shear mixer and granulated using purified water.
2. The wet granules are dried in a fluid bed drier, passed through a screen and then subjected to sizing.
3. The colloidal silicon dioxide and the rest of the croscarmellose sodium are mixed, passed through a screen and blended with the granules of step 2.
4. The magnesium stearate is passed through a screen, blended with the blend of step 3 and the total mixture is compressed to tablets.

Example 2

Ingredient	**Quantity (wt/tablet) mg**
Nateglinide	121.21*
Lactose	343.79
Sodium lauryl sulphate	12.5
Povidone	12
Croscarmellose sodium	20
Colloidal silicon dioxide	16
Purified water	q.s
Croscarmellose Sodium	12.8
Colloidal silicon dioxide	12.8
Magnesium stearate	11.4

** Equivalent to Nateglinide 120mg after potency and moisture adjustment*

PROCEDURE:

1. Nateglinide along with lactose, sodium lauryl sulphate, povidone, colloidal silicon dioxide and a part of croscarmellose sodium are mixed in a high shear mixer and granulated using purified water.

2. The wet granules are dried in a fluid bed drier, passed through a screen and then subjected to a sizing.
3. The colloidal silicon dioxide and the rest of the croscarmellose sodium are mixed, passed through a screen and blended with the granules of step 2.
4. The magnesium stearate is passed through a screen, blended with the blend of step 3 and the total mixture is compressed to tablets.

Example 3

Ingredient	**Quantity (wt/tablet) mg**
Nateglinide	121.21*
Lactose	343.79
Polysorbate 80	12.5
Povidone	12
Croscarmellose sodium	20
Colloidal silicon dioxide	16
Purified water	q.s
Croscarmellose Sodium	12.8
Colloidal silicon dioxide	12.8
Magnesium stearate	11.4

** Equivalent to Nateglinide 120mg after potency and moisture adjustment*

PROCEDURE:

1. Nateglinide along with lactose, polysorbate 80, povidone, colloidal silicon dioxide and a part of croscarmellose sodium are mixed in a high shear mixer and granulated using purified water.
2. The wet granules are dried in a fluid bed drier, passed through a screen and then subjected to a sizing.
3. The colloidal silicon dioxide and the rest of the croscarmellose sodium are mixed, passed through a screen and blended with the granules of step 2.
4. The magnesium stearate is passed through a screen, blended with the blend of step 3 and the total mixture is compressed to tablets.

Example 4

Ingredient	Quantity (wt/tablet) mg
Nateglinide	120
Microcrystalline cellulose	425
Povidone	12
Croscarmellose sodium	20
Colloidal silicon dioxide	16
Purified water	q.s
Croscarmellose Sodium	12.8
Colloidal silicon dioxide	12.8
Magnesium stearate	11.4

PROCEDURE:

1. Nateglinide along with microcrystalline cellulose, povidone, colloidal silicon dioxide and a part of croscarmellose sodium are mixed in a high shear mixer and granulated using purified water.
2. The wet granules are dried in a fluid bed drier, passed through a screen and then subjected to sizing.
3. The colloidal silicon dioxide and the rest of the croscarmellose sodium are mixed, passed through a screen and blended with the granules of step 2.
4. The magnesium stearate is passed through a screen, blended with the blend of step 3 and the total mixture is compressed to tablets.

Example 5

Ingredient	Quantity (wt/tablet) mg
Nateglinide	120
Microcrystalline cellulose	412.5
Sodium lauryl sulphate	12.5
Povidone	12

Croscarmellose sodium	10
Colloidal silicon dioxide	16
Purified water	q.s
Croscarmellose Sodium	22.8
Colloidal silicon dioxide	12.8
Magnesium stearate	11.4

PROCEDURE:

1. Nateglinide along with microcrystalline cellulose, sodium lauryl sulphate, povidone, colloidal silicon dioxide and a part of croscarmellose sodium are mixed in a high shear mixer and granulated using purified water.
2. The wet granules are dried in a fluid bed drier, passed through a screen and then subjected to a sizing.
3. The colloidal silicon dioxide and the rest of the croscarmellose sodium are mixed, passed through a screen and blended with the granules of step 2.
4. The magnesium stearate is passed through a screen, blended with the blend of step 3 and the total mixture is compressed to tablets.

Example 6

Ingredient	**Quantity (wt/tablet) mg**
Nateglinide	120
Microcrystalline cellulose	412.5
Polysorbate 80	12.5
Povidone	12
Croscarmellose sodium	10
Colloidal silicon dioxide	16
Purified water	q.s
Croscarmellose Sodium	22.8
Colloidal silicon dioxide	12.8
Magnesium stearate	11.4

PROCEDURE:

1. Nateglinide along with microcrystalline cellulose, polysorbate 80, povidone, colloidal silicon dioxide and a part of croscarmellose sodium are mixed in a high shear mixer and granulated using purified water.
2. The wet granules are dried in a fluid bed drier, passed through a screen and then subjected to a sizing.
3. The colloidal silicon dioxide and the rest of the croscarmellose sodium are mixed, passed through a screen and blended with the granules of step 2.
4. The magnesium stearate is passed through a screen, blended with the blend of step 3 and the total mixture is compressed to tablets.

Comparative *In vitro* dissolution study

In vitro release of nateglinide from tablets as per composition of Example 1-6 was studied in 1000 ml, 0.01 N HCl, with 0.5% SLS (pH–1.2), using USP apparatus – II, at 50 rpm. The results are listed in Table 1 and Table 2.

Table 1: In vitro release of nateglinide from tablets

Time	Cumulative percentage (%) release of nateglinide from Tablets			
	STARLIX	Example 1	Example 2	Example 3
10	62	40	50	54
20	-	43	-	71
30	65	72	71	80
45	67	77	81	87
60	72	-	-	-
Infinity	93	96	98	96

Table 2: In vitro release of nateglinide from tablets

Time	Cumulative percentage (%) release of nateglinide from Tablets			
	STARLIX	Example 4	Example 5	Example 6
10	62	-	-	-
15	-	38	51	66
30	65	46	67	80
45	67	54	75	87
60	72	69	-	-
Infinity	93	-	96	96

Table 1 and 2 clearly indicates that compositions with surfactants (Example 2, 3, 5 and 6) show a better dissolution profile as compared to compositions without surfactant (Example 1 and 4).

While there has been shown and described what are the preferred embodiments of the invention, one skilled in the pharmaceutical formulation art will appreciate that various modifications in the formulations and process can be made without departing from the scope of the invention as it is defined by the appended claims.

WE CLAIM:

1. A oral solid composition of Nateglinide comprising:

   a) Nateglinide or pharmaceutically acceptable salts thereof; and

   b) at least one pharmaceutically acceptable surfactant,

2. The oral solid composition of Nateglinide according to claim 1 wherein the surfactant is selected from a group of anionic, nonionic or cationic or a combination thereof.

3. The oral solid composition of Nateglinide according to claim 2 wherein the surfactant is selected from anionic surfactants such as sodium lauryl sulphate, potassium dodecyl sulphonate, sodium dodecyl benzene sulphonate, sodium salt of lauryl polyoxyethylene sulphate, lauryl polyethylene oxide sulfonate, dioctyl ester of sodium sulphosuccinic acid or sodium lauryl sulphonate and combinations thereof.

4. The oral solid composition of Nateglinide according to claim 2 wherein the surfactant is selected from nonion ic surfactants such as polysorbate 80, nonyl phenol polyoxyethylene ether, tridecyl alcohol polyoxyethylene ether, dodecyl mercaptan polyoxyethylene thioether, the lauric ester of polyethylene glycol, the lauric ester of sorbitan polyoxyethylene ether or tertiary alkyl amine oxide and combinations thereof.

5. The oral solid composition of Nateglinide according to claim 2 wherein the surfactant is selected from cationic surfactants such as distearyl dimethyl ammonium chloride, stearyl dimethyl benzyl ammonium chloride, stearyl trimethyl ammonium chloride, coco dimethyl benzyl ammonium chloride, dicoco dimethyl ammonium chloride, cetyl pyridinium chloride, cetyl trimethyl ammonium bromide, stearyl amine salts that are soluble in water such as stearyl amine acetate and stearyl amine hydrochloride, stearyl dimethyl amine hydrochloride, distearyl amine hydrochloride, alklyl phenoxyethoxyethyl dimethyl ammonium chloride, decyl pyridinium bromide, pyridinium chloride derivative of the acetyl amino ethyl esters of lauric acid, lauryl trimethyl ammonium chloride, decyl amine acetate, lauryl

dimethyl ethyl ammonium chloride, the lactic acid and citric acid and other acid salts of stearyl-1-amidoimidazoline with methyl chloride, benzyl chloride, chloroacetic acid and similar compounds, and combinations thereof.

6. The oral solid composition of Nateglinide according to claim 3 wherein the surfactant is sodium lauryl sulphate.

7. The oral solid composition of Nateglinide according to claim 4 wherein the surfactant is polysorbate 80.

8. The oral solid composition of Nateglinide according to claim 1 wherein in addition to Nateglinide and surfactant, it comprises of other pharmaceutically acceptable excipients selected from a group consisting of filler, binder, disintegrant, lubricant, coloring and flavoring agent.

9. The oral solid composition according to claim 8 wherein filler is selected from the group comprising of corn starch, lactose, white sugar, sucrose, sugar compressible, sugar confectioners, glucose, sorbitol, calcium carbonate, calcium phosphate-dibasic, calcium phosphate-tribasic, calcium sulfate, microcrystalline cellulose, silicified microcrystalline cellulose, cellulose powdered, dextrates, dextrins, dextrose, fructose, kaolin, lactitol, mannitol, sorbitol, starch, starch pregelatinized, sucrose, and mixtures thereof.

10. The oral solid composition according to claim 9 wherein filler is lactose.

11. The oral solid composition according to claim 9 wherein filler is microcrystalline cellulose.

12. The oral solid composition according to claim 8 wherein binder is selected from methyl cellulose, hydroxypropyl cellulose, polyvinylpyrrolidone, gelatin, gum Arabic, ethyl cellulose, polyvinyl alcohol, pullulan, pregelatinized starch, agar, tragacanth, sodium alginate, propylene glycol, and mixtures thereof.

13. The oral solid composition according to claim 12 wherein binder is polyvinylpyrrolidone.

14. The oral solid composition according to claim 8 wherein disintegrant is selected from starch, croscarmellose sodium, crospovidone, sodium starch glycolate and mixtures thereof.

15. The oral solid composition according to claim 14 wherein disintegrant is croscarmellose sodium.

16. The oral solid composition according to claim 8 wherein lubricant is selected from colloidal anhydrous silica, stearic acid, magnesium stearate, calcium stearate, talc, hydrogenated castor oil, sucrose esters of fatty acids, microcrystalline wax, yellow beeswax, white beeswax and mixtures thereof.

17. The oral solid composition according to claim 16 wherein lubricant is magnesium stearate.

18. The oral solid composition according to claim 1 wherein it is in the form of a tablet.

19. The oral solid composition according to claim 1 wherein it is in the form of a capsule.

20. The oral solid composition according to claim 18 wherein the tablet is further coated with one or more functional and/or non-functional layers.

21. A process for preparation of oral tablets of Nateglinide comprising:

a) Nateglinide or pharmaceutically acceptable salts thereof; and

b) at least one pharmaceutically acceptable surfactant,

by wet granulation, dry granulation or direct compression.

22. A process for preparation of oral tablets of Nateglinide according to claim 21 wherein in addition to Nateglinide and surfactant, it also comprises of other pharmaceutically acceptable excipients.

23. A process for preparation of oral tablets of Nateglinide according to claim 22 wherein other pharmaceutically acceptable excipients are selected from a group consisting of filler, binder, disintegrant, lubricant, coloring and flavoring agent.

24. The process for preparation of oral tablets of Nateglinide according to claim 23, by blending Nateglinide, surfactant, filler and disintegrant; granulating the blend with a binder solution; drying the granules; sizing; lubricating and compressing the lubricated granules.

25. The process for preparation of oral tablets of Nateglinide according to claim 23, by blending Nateglinide, surfactant, filler, disintegrant and binder; granulating the

blend with a solvent; drying the granules; sizing; lubricating and compressing the lubricated granules.

26. The process for preparation of oral tablets of Nateglinide according to claim 23, by blending Nateglinide, surfactant, filler, disintegrant and binder; compacting or slugging the blend; breaking the slugs to make granules; lubricating and compressing the lubricated granules.

27. The process for preparation of oral tablets of Nateglinide according to claim 23, by blending nateglinide, surfactant, filler, disintegrant, binder and lubricant; and compressing.

28. A medicament for the prevention, delay of progression or treatment of metabolic disorders, in particular of type 2 diabetes mellitus or a disease or condition associated with diabetes mellitus comprising:

    a) Nateglinide or pharmaceutically acceptable salts thereof; and

    b) at least one pharmaceutically acceptable surfactant.

29. A oral solid composition of Nateglinide comprising:

    a) Nateglinide or pharmaceutically acceptable salts thereof; and

    b) at least one pharmaceutically acceptable surfactant,

as described and illustrated herein.

Dated this **28TH** day of **November, 2003.**

For Ranbaxy Laboratories Limited

(Sushil Kumar Patawari)
Company Secretary